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CONNOLLY BOVE LODGE & HUTZ, LLP
P O BOX 2207
WILMINGTON, DE 19899

EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,954	SCHMITZ ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *3,6 and 18-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5 and 7-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/05, 11/05, 11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/EP03/14649.

Claims 1-25 are currently pending.

The preliminary amendment filed on 6/1/2007, amending claims 2-4, and 18-20 is acknowledged.

Applicant's election with traverse of Group I, Claims 1-2 and 4-17, drawn to a process for preparing amino acids in an organism comprising introducing a gene encoding threonine degrading protein, and the protein of SEQ ID NO: 2 in the response filed on 12/1/2006 is acknowledged.

The traversal is on the ground(s) that lack of unity established by the Examiner is not proper. Applicants argue that the reference cited by the Examiner, Monschau et al., teaches an *Ashbya* threonine aldolase and the GenBank Accession No. AAL52676, discloses lysine decarboxylase from Brucella melitensis, wherein neither reference teaches the production of genetically modified organisms for the preparation of amino acids, and none of the references teaches that an increase *of Saccharomyces cerevisiae* (yeast) threonine aldolase (SEQ ID NO: 2) leads to an increased production of methionine, homoserine and lysine. This is not found persuasive because the shared technical feature of all the groups is either threonine degrading protein or lysine degrading protein; and SEQ ID NO: 2 is not the shared special technical feature in all claims. However, Monschau et al. teach threonine aldolase which degrade threonine, which is 99.8% identical to threonine degrading protein of the instant application (SEQ ID NO: 2). Therefore, the shared technical feature "threonine degrading protein" does not make contribution

over the prior art. Regarding, vector of claim 19, which grouped with nucleic acid, should not be included in the elected group, although there may be common use. Similarly, transformed transgenic organism also grouped with nucleic acid, should not be included with the elected group. Applicants are reminded that Special technical feature of an International or 371 Application designed for restriction requirement, wherein the special technical feature is common to all the groups. If the special technical feature is unique, novel and non-obvious, then Unity of invention occurs, in that situation, nucleic acid, polypeptide, method of producing polypeptide and method of using (only one) said polypeptide or polynucleotide should be examined together. If that special technical feature is known, there is no unity of invention and only elected groups should be examined. Applicants further traversed the restriction requirement of independent and distinct proteins of SEQ ID NOs: 2, 3, 4, 5, 6, 7, 8, 9, 10, 14 and 16 (threonine aldolase), and SEQ ID NOs: 12, 18, 20, 22, 24 and 26 (lysine decarboxylase) that is not persuasive because the proteins of said SEQ IDs are unrelated, and different proteins of said SEQ IDS, which are polypeptides of threonine aldolase or lysine decarboxylase, do not have special technical feature among each other because they all represent structurally different polypeptides and polynucleotide encoding them. As mentioned above, a polypeptide threonine aldolase or lysine decarboxylase is known in the art and does not make contribution over the prior art. Therefore, they all lack special technical feature at the same time lack unity of invention. Besides, searching all the groups and all the sequences would create a serious search burden to the Examiner because searching all the groups require nucleic acid sequence, and protein sequence search, which includes mutants and variants as well as Patent and non-Patent literature search, which would create a serious burden to the Office.

As restriction is clearly permissible even among related inventions as defined in MPEP 808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 3, 6, 18-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-2, 45, 7-17 are under consideration and are being examined herein.

Priority

Acknowledgement is made of applicants claim for priority of foreign application GERMANY 10261188.2 filed on 12/20/2002.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 11/18/2005, 11/7/2005, 6/17/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are considered by the examiner. The signed copies of IDS are enclosed herewith.

Drawings

There is no drawing with this application.

Claim Objections

Claims 1, and 5 are objected to as encompassing non-elected subject matter. Appropriate correction is requested.

Claims 2, 4, 5, and 7-17 are objected to because of the recitation "A process ---", which actually depends from claim 1. Examiner suggests amending claims to recite "The process ---". Appropriate correction is requested.

Claims 2, and 4 are objected to because of the recitation "wherein the process comprises the following steps, solved", which should be "wherein the process comprises the following steps". Appropriate correction is requested.

Claims 1, 2 and 4 are objected to because of the recitation "which codes for", which should be "encoding". Appropriate correction is requested.

Claim 11 is objected to because of the following informalities: Bacterial species names should be italicized. Appropriate correction is requested.

Claims 4 and 6-10, are objected to because of the following informalities: "wherein genes encoding ---- is cloned" is grammatically incorrect and should be "wherein the gene encoding-----is cloned". Appropriate correction is required.

Claim 16 is objected to because of the recitation "nucleic acid sequence is for introduction and for expression incorporated into nucleic acid" is grammatically awkward. It is suggested, this phrase be replaced with "the nucleic acid sequence is incorporated into a nucleic acid construct or vector for introduction and expression in said transgenic organism".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 5 is indefinite in the recitation "degeneracy of genetic code", which is confusing. What structure does the threonine aldolase encompass due to degeneracy of the genetic code? Does threonine aldolase have same amino acid sequence compared to the wild type protein or does it has something else?

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is indefinite in the recitation "which codes for ----- SEQ ID NO: 2 and have at least 50% homology" is unclear. A protein cannot be simultaneously SEQ ID NO: 2 and a variant of SEQ ID NO: 2.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is indefinite in the recitation "negligible", which is confusing. The metes and bounds of the term "negligible" are not clear to the Examiner. It is not clear as to how one skilled in the art can know what negligible mean in terms of activity.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is indefinite in the recitation of "biological activity" as it is unclear what the scope of activities that is encompassed by this term. The specification does not define this term with a specific meaning. One of ordinary skill in the art would not determine how much activity is encompassed by this term.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 5 recites "a derivative of the nucleic acid sequence depicted in SEQ ID NO: 1", which is confusing as to the scope of nucleic acid sequence of SEQ ID NO: 1. It is not clear whether this phrase includes structural derivatives of SEQ ID NO: 1 having functional activity or not. Similarly, the term "derivative" is confusing, as no guidance is provided as to the manner in which a derivative is related to the claimed polynucleotide. Clarification is required.

Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 14 and 15 recite the phrase "derived from a eukaryote --- or genus Saccharomyces ---". The metes and bounds of this phrase are not clear to the examiner because "derived" imply the genes including wild type as well as mutants, variants or fragments, which are unknown, thereby rendering the scope of the claim(s) indefinite. The recitation "derived" can be replaced with "isolated".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4, and 7-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 4 and 7-17 are directed to a process for preparing amino acids in transgenic organism, wherein the process comprises introduction of a nucleic acid sequence encoding a threonine-degrading protein or increasing threonine-degradation (claim 1 and 2) having a consensus sequence of SEQ ID NO: 27 or 28 (claim 4), wherein said nucleic acid sequence depicted in SEQ ID NO: 1 encoding said protein of SEQ ID NO: 2 or a nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or a nucleic acid which is derivative of SEQ ID NO: 1.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical*).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v.*

G.D. Searle & Co. the methods were held to lack written description because not a single example of the product used in the claimed methods was described (this is in contrast to the few examples of microorganism useable in the claimed methods), the same analysis applies wherein the product, used in the claimed methods, must have adequate written description (see *Enzo* paraphrase above).

Thus, claims 1-2, 4 and 7-17 are drawn to a process for preparing amino acids in transgenic organism, wherein the process comprises introduction of a nucleic acid sequence encoding a threonine-degrading protein or increasing threonine-degradation (claim 1 and 2) having a consensus sequence of SEQ ID NO: 27 or 28 (claim 4), wherein said nucleic acid sequence depicted in SEQ ID NO: 1 encoding said protein of SEQ ID NO: 2 or a nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or a nucleic acid which is derivative of SEQ ID NO: 1. Claims are drawn to a process of using a threonine-degrading enzyme whose structure is not fully described in the specification. No information, beyond the characterization of gene encoding threonine aldolase having a nucleic acid sequence of SEQ ID NO: 1 has been provided, which would indicate that they had possession of the claimed genus of any threonine degrading enzyme. The specification does not contain any disclosure of the structures of all the mutants or variants of any threonine-degrading enzyme within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including mutants and variants, which can have wide variety of structures. Therefore, many structurally unrelated polypeptides are encompassed within the scope of the method of the claims. The specification discloses the structure of only a single representative species of the claimed genus i.e. SEQ ID NO: 1, which is insufficient to put one of skill in the art in possession

of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-2, 4-5 and 7-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for preparing amino acid methionine in transgenic organism including C. glutamicum and A. thaliana, wherein the process comprises introduction of a nucleic acid sequence of SEQ ID NO: 1 encoding a threonine-degrading protein threonine aldolase of SEQ ID NO: 2 from S. cerevisiae having a consensus sequence of SEQ ID NO: 27 or 28, does not reasonably provide enablement for a process for preparing amino acids in any transgenic organism, wherein the process comprises introduction of a nucleic acid sequence encoding any threonine-degrading protein (claims 1-2), or any nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequence which is any derivative of SEQ ID NO: 1 or any nucleic acid sequence encoding any protein having at least 50% homology to SEQ ID NO: 2 (claim 5). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, **to make and use** the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731,737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows:

(1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5)

the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The factors, which have, lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed below:

The breath of the claims:

Claims 1-2, and 4-5 are so broad as to encompass a process for preparing amino acids in any transgenic organism, wherein the process comprises introduction of a nucleic acid sequence encoding any threonine-degrading protein (claims 1-2), or any nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequence which is any derivative of SEQ ID NO: 1 or any nucleic acid sequence encoding any protein having at least 50% homology to SEQ ID NO: 2 (claim 5). Claim 7 recites the process, wherein the transgenic organism is cultivated and harvested after expression of said nucleic acid and claim 8 recites the process for preparing amino acids in transgenic organisms as claimed in claim 1, wherein the amino acid is isolated from the organism or the culture medium or the organism and the culture medium. Claim 9 recites the process, wherein the essential amino acid methionine is involved and claim 10 recite the process, wherein the transgenic organism is a microorganism or a plant. Claim 11 recites the process, wherein the transgenic organism is a microorganism selected from the group of genera Corynebacterium, Brevibacterium, Escherichia, Bacillus, Rhodotorula, Hansenula, Schizosaccharomyces, Saccharomyces, Candida, Claviceps or Flavobacterium and claim 12 recites the process, wherein the transgenic organism is a plant selected from the group of crop plants. Claim 13 recites the process, wherein the transgenic organism is a plant selected from the group of peanut, oilseed rape, canola, sunflower, safflower,

olive, sesame, hazelnut, almond, avocado, bay, pumpkin, lettuce, flax, soybean, pistachio, borage, corn, wheat, rye, oats, millet, triticale, rice, barley, cassava, potato, sugar beet, feed beet, aubergine, tomato, pea, alfalfa and perennial grasses and feed crops and claim 14 recites the process wherein the nucleic acid sequence is derived from a eukaryote. Claim 15 recites the process, wherein the nucleic acid sequence is derived from the genus Saccharomyces and claim 15 recites the process, wherein the nucleic acid is for introduction and for expression, incorporated into a nucleic acid construct or a vector. Claim 17 recites the process, wherein additionally biosynthesis genes of the amino acid prepared in the process are introduced into the organism.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid sequences encoding any threonine-degrading protein (claims 1-2), or any nucleic acid sequences obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequences which is any derivative of SEQ ID NO: 1 or any nucleic acid sequences encoding any protein having at least 50% homology to SEQ ID NO: 2 (claim 5), which includes many mutants and variants used in the claimed method. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one threonine degrading protein i.e. threonine aldolase of SEQ ID NO: 2 encoded by SEQ ID NO: 1 used in the claimed method.

The amount of direction or guidance presented and the existence of working examples:

The specification discloses a process for preparing amino acid methionine in transgenic organism including C. glutamicum and A. thaliana, wherein the process comprises introduction of a nucleic acid sequence of SEQ ID NO: 1 encoding a threonine-degrading protein threonine

aldolase of SEQ ID NO: 2 from S. cerevisiae having a consensus sequence of SEQ ID NO: 27 or 28. However, the specification fails to provide any clue as to the structural elements required in any nucleic acid sequences encoding any threonine-degrading protein, or any nucleic acid sequences obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequences which is any derivative of SEQ ID NO: 1 or any nucleic acid sequences encoding any protein having at least 50% homology to SEQ ID NO: 2, which includes many mutants and variants used in the claim method or which are the structural elements in said proteins to be used in the claimed method known in the art that are essential for successfully practice the claimed process of preparing amino acid. No correlation between structure and function has been presented.

The specification does not support the broad scope of the claims which encompass any nucleic acid sequences encoding any threonine-degrading protein, or any nucleic acid sequences obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequences which is any derivative of SEQ ID NO: 1 or any nucleic acid sequences encoding any protein having at least 50% homology to SEQ ID NO: 2 used in claimed method because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting threonine aldolase activity and; (B) the general tolerance of threonine aldolase polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying threonine aldolase polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for preparing any amino acids in any transgenic organism, wherein the process comprises introduction of any nucleic acid sequence encoding any threonine-degrading protein, or any nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequence which is any derivative of SEQ ID NO: 1 or any nucleic acid sequence encoding any protein having at least 50% homology to SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a process for preparing amino acids in any transgenic organism by introducing of a nucleic acid sequence encoding any threonine-degrading protein, or any nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequence which is any derivative of SEQ ID NO: 1 or any nucleic acid sequence encoding any protein having at least 50% homology to SEQ ID NO: 2 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art:

The amino acid sequence of a polypeptide determines its structural and functional properties. While the specification discloses a single Saccharomyces cerevisiae threonine aldolase of SEQ ID NO: 2 encoded by nucleic acid sequence of SEQ ID NO: 1, neither the

specification nor the art provide a correlation between structure and function such that one of skill in the art can envision the structure of any nucleic acid sequence encoding any threonine-degrading protein, or any nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequence which is any derivative of SEQ ID NO: 1 or any nucleic acid sequence encoding any threonine degrading protein having at least 50% homology to SEQ ID NO: 2 used in a process to prepare amino acid. The art clearly teaches that modification of a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are tolerant of modification and which ones are conserved is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (1999) and Seffernick et al. (2001), where it is shown that even small amino acid changes result in enzymatic activity changes.

The quantity of experimentation required practicing the claimed invention based on the teachings of the specification:

While methods of generating or isolating variants of a polynucleotide were well known in the art at the time of invention, it is not routine in the art to screen by trial and error process for

(1) all nucleic acids encoding any threonine degrading or any nucleic acid sequence obtained owing to the degeneracy of genetic code of SEQ ID NO: 1 or any nucleic acid sequence which is any derivative of SEQ ID NO: 1 or any nucleic acid sequence encoding any threonine degrading protein having at least 50% homology to SEQ ID NO: 2, (2) an essentially infinite number of mutations of any gene encoding any threonine degrading protein sequence. The amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

Conclusion:

Therefore, taking into consideration of the extremely broad scope of the claims, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and function, and the high degree of unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5, 7, 10, 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS). Instant claims are drawn to a process for producing amino acid such as methionine, homoserine or lysine in transgenic organism including microorganism, wherein said microorganism is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity isolated from Saccharomyces cerevisiae.

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase from S. cerevisiae, which degrade threonine, which is 99.8% identical to SEQ ID NO: 2 of the instant application, wherein the process produces amino acid glycine. Monschau et al. further teach that the threonine degrading protein (threonine aldolase) comprises consensus sequences of SEQ ID NO: 27 and 28 (claim 2), which are 100% identical to SEQ ID NO: 27 and 28 of the instant application. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism. Therefore, Monschau et al. anticipate claims 1, 2, 5, 7, 10, and 14-16 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 11 is rejected under 35 U.S.C. 103(a) as obvious over Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS). Instant claims are drawn to a process for producing amino acid in transgenic organism including

microorganism such as Saccharomyces cerevisiae, wherein said microorganism is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity. Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase which degrade threonine, which is 99.8% identical to SEQ ID NO: 2 of the instant application, wherein the process produce amino acid glycine. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism. Monschau et al. do not teach using fungal strain Saccharomyces for producing said L-amino acids.

It would have been obvious to one of ordinary skill in the art to use fungal strain Saccharomyces instead of fungal strain A. gossypii, which is well-known host cell in the art.

One of ordinary skill in the art would have been motivated to do so because fungal strain Saccharomyces is readily available, well known, easy to grow and inexpensive fungal strain widely used in the art.

One of ordinary skill in the art would have a reasonable expectation of success because threonine aldolase gene is isolated from S. cerevisiae and using S. cerevisiae as host cell for producing enhanced threonine aldolase enzyme in order to producing enhanced glycine would be highly expected.

Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS) as applied to claims 1, 2, 5, 7-8, 10-11, and 14-16 above, and further in view of

Castigioni et al. (US PGPUB 2005/0160500 A1, publication 7/21/2005, claim priority of 60/467,910 filed on 7/15/2003). Instant claim is drawn to a process for producing amino acid in transgenic organism including transgenic plant, wherein said organism is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity.

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase from S. cerevisiae, which degrade threonine, which is 99.8% identical to SEQ ID NO: 2 of the instant application, wherein the process produces amino acid glycine. Monschau et al. further teach that the threonine degrading protein (threonine aldolase) comprises consensus sequences of SEQ ID NO: 27 and 28 (claim 2), which are 100% identical to SEQ ID NO: 27 and 28 of the instant application. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism. Monschau et al. do not teach using transgenic plant to produce amino acids.

Castigioni et al. teach a plant cell transformed with a gene, which increase glycine-betaine, an analogue of amino acid glycine. Castigioni et al. further teach regeneration of a transgenic plant from plant cell, wherein the plants are soy, cotton, canola, wheat, sunflower, sorghum, alfalfa, barley, millet, rice, tobacco, fruit and vegetable crops, and turf grass, wherein preferred crop plant is Zea mays, commonly known as maize or corn.

By combining the teachings of Monschau et al. and Castigioni et al. it would have been obvious to one to ordinary skill in the art at the time of the invention was made to use transgenic plant as taught by Castigioni et al. in the method of Monschau et al. to produce amino acid.

One of ordinary skill in the art would have been motivated to use plant to produce amino acid because plant is readily available, easy to grow, easy to maintain and plant can be used for industrial production of said amino acids in agricultural industry.

One of ordinary skill in the art would have a reasonable expectation of success because Castigioni et al. successfully used transgenic plant for producing glycine-betaine.

Therefore, claims 12 and 13 would have been *prima facie* obvious to use one of ordinary skill in the art.

Although, the date of Castigioni et al. reference is after the foreign priority date of the instant application, the foreign priority date of the instant application is not granted because it is not in English language.

Conclusion

Status of the claims:

Claims 1-25 are pending.

Claims 3, 6 and 18-25 are withdrawn.

Claims 1-2, 4-5, and 7-17 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Iqbal Chowdhury, PhD, Patent Examiner
Art Unit 1652 (Recombinant Enzymes)
US Patent and Trademark Office
Rm. REM 2B69, Mail Box. 2C70
Ph. (571)-272-8137, Fax. (571)-273-8137

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PRIMARY EXAMINER
GROUP ~~1600~~ 1652